# AMENDMENTS

## Amendments to the Claims:

Please amend the claims as follows, without prejudice.

## In the Claims:

1-36. Cancelled.

37. (Currently Amended) A method of determining the activity of an enzyme~~, or the effect a test compound has on the activity of the enzyme,~~ by using mass spectroscopy comprising the steps of:

(i) providing a probe carrying an immobilised enzyme;

(ii) optionally introducing ~~the~~ a test compound;

(iii) introducing one or more reactants to the immobilised enzyme for a time, and in a form sufficient for a reaction to take place;

(iv) drying the probe;

(v) subjecting the probe to mass spectroscopy;

(vi) determining the activity of the enzyme, ~~or the effect the test compound had on the activity of the enzyme,~~ by detecting the presence and/or absence of one or more products and/or the one or more reactants; wherein ~~characterised in that~~ a layer resistant to non-specific protein binding comprising protein repellent molecules is provided on the probe surface.

38. (Currently Amended) The method of claim 37, wherein said ~~layer resistant to non-specific protein binding comprises~~ protein repellent ~~molecules such as~~ is selected from the group consisting of ~~are~~ polyethylene glycol, dextran, polyurethane, polyacrylamide ~~or~~ and self-assembled monolayers molecules~~, which protein repellent molecules are~~ immobilised on the probe surface.

39. (Currently Amended) The method of claim 37, wherein the enzyme is a kinase ~~such as~~ selected from the group consisting of a serine kinase, threonine kinase, tyrosine kinase or non-protein kinase or an oxidoreductase, a transferase, a hydrolase, a lyase, a ligase, a carboxylase, an esterase, a phosphodiesterase, a protein phosphatase such as a tyrosine phosphatase, a G-protein coupled receptor, an ATP-dependent chaperone, a cyclooxygenase, a cytochrome P450, a sialidase, a short-chain dehydrogenase, a short-chain reductase, and ~~or~~ an isomerase.

40. (Currently Amended) The method of claim 37 for determining the activity of one or more kinases ~~or the effect a test compound has on the activity of one or more kinases~~ by using MALDI mass spectroscopy.

41. (Previously Presented) The method of claim 40, wherein the one or more reactants comprise a phosphate donor, a phosphate acceptor and a divalent cation.

42. (Currently Amended) The method of claim 41, wherein the phosphate donor is a phosphorylated substrate and the phosphate acceptor is a nucleotide ~~di phosphate~~ diphosphate (NDP).

43. (Currently Amended) The method of claim 41, wherein the phosphate donor is a nucleotide ~~tri phosphate~~ triphosphate (NTP) and the phosphate acceptor is a substrate to be phosphorylated.

44. (Previously Presented) The method of claim 41, wherein the divalent cation is magnesium or manganese.

45. (Currently Amended) The method of claim 42, wherein the nucleotide ~~di phosphate~~ diphosphate or ~~tri phosphate~~ triphosphate is an ~~adenine di~~ adenine diphosphate or adenine triphosphate ~~tri phosphate~~.

46. (Currently Amended) The method of claim 37, wherein the detected product is a nucleotide ~~tri phosphate~~ triphosphate or a nucleotide ~~di phosphate~~ diphosphate ~~and its presence is detected~~.

47. (Currently Amended) The method of claim 46, wherein the nucleotide ~~tri phosphate~~ triphosphate or nucleotide ~~di phosphate~~ diphosphate are detected as $[NDP]^-$ or $[NTP]^-$ or as one or more adduct peaks thereof.

48. (Previously Presented) The method as claimed in claim 47, wherein the one or more adduct peaks are adduct peaks with a monovalent cation ($M^+$).

49. (Currently Amended) The method of claim 48, wherein the one or more adduct peaks is selected from the group comprising $[ATPM]^-$, $[ATPM_2]^-$ ,~~and~~ $[ATPM_3]^-$ ,~~and/or~~ $[ADPM]^-$, $[ADPM_2]^-$, and $[ADPM_3]^-$.

50. (Previously Presented) The method of claim 37, further comprising, between step (iv) and step (v), the step of overlaying the probe with energy absorbing molecules.

51. (Previously Presented) The method of claim 50, wherein said energy absorbing molecules are deposited onto the probe surface in a non-aqueous solvent, followed by evaporation of the solvent.

52. (Previously Presented) The method of claim 37, wherein said probe carries more than one enzyme.

53. (Previously Presented) The method of in claim 37, wherein in step (iii) said one or more reactants are added in the presence of a low salt buffer.

54. (Currently Amended) The method of claim 53, wherein said low salt buffer is a semi-volatile buffer. ~~such as ammonium bicarbonate buffer.~~

55. (Cancelled)

56. (Currently Amended) The method of claim 37, wherein the enzymes are attached to the probe as fusion proteins ~~typically via~~ with a tag.

57. (Previously Presented) The method of claim 37, wherein said test compound is added before, after or with the one or more reactants to determine its effect on enzyme activity.

58. (Currently Amended) The method of claim 37, wherein the mass spectroscopy is a laser desorption ionisation mass spectroscopy. ~~preferably a MALDI mass spectrometry.~~

59. (Previously Presented) The method of claim 37, wherein the one or more reactants and the optional test compound are introduced to the immobilised enzyme as a droplet, such as a droplet having a volume of less than 1 microliter.

60. (Withdrawn) A probe for use with a mass spectrometer in the method of claim 37, comprising a support having an electroconductive surface thereon, characterised in that the target surface comprises an array having a plurality of enzymes immobilised thereon, and in that the probe surface is provided with a layer resistant to non-specific protein binding.

61 (New) The method of claim 53, wherein said low salt buffer is an-ammonium bicarbonate buffer.

62 (New) The method of claim 37, wherein said mass spectroscopy is a MALDI mass spectrometry.

63. (New) A method of determining the effect a test compound has on the activity of the enzyme, by using mass spectroscopy comprising the steps of:

(i) providing a probe carrying an immobilised enzyme;

(ii) introducing a test compound;

(iii) introducing one or more reactants to the immobilised enzyme for a time, and in a form sufficient for a reaction to take place;

(iv) drying the probe;

(v) subjecting the probe to mass spectroscopy;

(vi) determining the effect the test compound had on the activity of the enzyme, by detecting the presence and/or absence of one or more products and/or the one or more reactants;

wherein a layer resistant to non-specific protein binding comprising protein repellent molecules is provided on the probe surface.

64. (New) A method of claim 63 wherein the effect of a test compound on the activity of one or more kinases using MALDI mass spectrometry is determined.

65. (New) A method of claim 63 wherein the effect of a test compound on the activity of one or more enzymes using MALDI mass spectrometry is determined wherein the enzyme is selected from the group consisting of a serine kinase, threonine kinase, tyrosine kinase or non-protein kinase or an oxidoreductase, a transferase, a hydrolase, a lyase, a ligase, a carboxylase, an esterase, a phosphodiesterase, a protein phosphatase such as a tyrosine phosphatase, a G-protein coupled receptor, an ATP-dependent chaperone, a cyclooxygenase, a cytochrome P450, a sialidase, a short-chain dehydrogenase, a short-chain reductase, and an isomerase.